9/17/96

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 NEWS  3  Aug  4  Macintosh STN Express Users of C(O)CH3 Shortcut
 NEWS  4  Jul 30  Use SDI EDIT to Change SDIs
 NEWS  5  Jul 30  Use SET ACCOUNT to Specify and Modify Online Cost
                  Centers
 NEWS  6  Jul 30  Use EDIT QUERY to Edit and Modify Online Queries
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 NEWS 13  Sep  9  Variable SDIs in API

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FILE LAST UPDATED: 17 Sep 1996  (960917/ED)

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=> s schott/au
L1             0 SCHOTT/AU

=> s schott?/au
L2          1532 SCHOTT?/AU
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```
=> s l2 and dota or dtpa
          195 DOTA
         5135 DTPA
L3       5135 L2 AND DOTA OR DTPA

=> s l2 and (dota or dtpa)
          195 DOTA
         5135 DTPA
L4          0 L2 AND (DOTA OR DTPA)

=> s l2 and chelat?
        72670 CHELAT?
L5          7 L2 AND CHELAT?

=> s l5 and radio isotop?
         35934 RADIO
        163837 ISOTOP?
           201 RADIO ISOTOP?
                 (RADIO(W)ISOTOP?)
L6          0 L5 AND RADIO ISOTOP?

=> d l5 ibib ab 1-

L5   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 1996 ACS
ACCESSION NUMBER:        1994:215313  CAPLUS
DOCUMENT NUMBER:         120:215313
TITLE:                   Vicinal diol linking agents for antibody
                         fragments and therapeutic agents
INVENTOR(S):             Frazier, Kevin A.; Schott, Margaret E.
PATENT ASSIGNEE(S):      Dow Chemical Co., USA
SOURCE:                  U.S., 18 pp. Cont.-in-part of U.S. Ser. No.
                         478,286, abandoned.
                         CODEN: USXXAM

                         NUMBER                  DATE
                         --------------          ------
PATENT INFORMATION:      US 5274119 A            931228
APPLICATION INFORMATION: US 91-677936            910401
PRIORITY APPLN. INFO.:   US 88-214247            880701
                         US 90-478286            900209
DOCUMENT TYPE:           Patent
LANGUAGE:                English
OTHER SOURCE(S):         MARPAT 120:215313
AB   A group of functionalized linking agents are disclosed. The linking
     agents contain thiol-reactive functionalities for covalent reaction
     with sulfhydryl groups from the hinge region of antibody fragments.
     The linking agents also contain masked aldehyde functionalities for
     covalent attachment of amine-contg. therapeutic agents by Schiff
     base formation. Carrier systems capable of delivering compds. to
     targeted sites in vivo based on antigen-antibody interactions are
     constructed from these linking agents. Thus, maleimido linking
     agent I was prepd. and used to further prep. a Fab-105Rh
   chelate mol. Prepn. of the chelate [105Rh complex
     with 6-(4-aminophenyl)methyl-1,4,8,11-tetraazoundecane] is also
     included.

L5   ANSWER 2 OF 7  CAPLUS  COPYRIGHT 1996 ACS
ACCESSION NUMBER:        1994:128617  CAPLUS
DOCUMENT NUMBER:         120:128617
TITLE:                   An improved linker for single-chain Fv with
                         reduced aggregation and enhanced proteolytic
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stability
AUTHOR(S): Whitlow, Marc; Bell, Brian A.; Feng, Sheau Line; Filpula, David; Hardman, Karl D.; Hubert, Steven L.; Rollence, Michele L.; Wood, James F.; **Schott, Margaret E.**; et al.
CORPORATE SOURCE: Protein Eng. Dep., Enzon, Inc., Piscataway, NJ, 08854-3998, USA
SOURCE: Protein Eng. (1993), 6(8), 989-95
CODEN: PRENE9; ISSN: 0269-2139
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of linker length on binding affinity and degree of aggregation have been examd. in the antifluorescein 4-4-20 and anticarcinoma CC49 single-chain Fvs. Longer linkers in the antifluorescein sFvs have higher affinities for fluorescein and aggregate less. A proteolytically susceptible site between Lys8 and Ser9, in the previously reported 212 linker has been identified. A new linker sequence, 218 (CSTSGSGKPGSGEGSTKG) was designed in which a proline was placed at the C-terminal side of the proteolytic clip site in the 212 linker. The CC49 sFv contg. the 218 linker showed reduced aggregation and was found to be more stable to proteolysis in vitro, when compared to the CC49/212 sFv. The CC49 sFv with the longer 218 linker had higher affinity than CC49/212 sFv. An aggregated CC49/212 sFv sample had higher affinity than CC49/218 sFv. The CC49/218 and CC49/212 sFvs had similar blood clearances in mice, while the aggregated CC49/212 sFv remained in circulation significantly longer. In mice bearing LS-174T human colon carcinoma xenografts, the CC49/218 sFv showed higher tumor uptake than the CC49/212 sFv and lower tumor uptake than the aggregated CC49/212 sFv. The higher tumor uptake of the CC49/218 is most likely a result of its higher resistance to proteolysis. The higher affinity and higher tumor uptake of the aggregated CC49/212 sFv are most likely due to the repetitive nature of the TAG-72 antigen and the higher avidity of multivalent aggregates. When the sFvs were radiolabeled with a lutetium-**chelate** the CC49/218 sFv showed a lower accumulation in the liver and spleen compared to the aggregated CC49/212 sFv.

L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1993:55232 CAPLUS
DOCUMENT NUMBER: 118:55232
TITLE: Differential metabolic patterns of iodinated versus radiometal **chelated** anticarcinoma single-chain Fv molecules
AUTHOR(S): **Schott, Margaret E.**; Milenic, Diane E.; Yokota, Takashi; Whitlow, Marc; Wood, James F.; Fordyce, William A.; Cheng, Roberta C.; Schlom, Jeffrey
CORPORATE SOURCE: Lab. Tumor Immunol. Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SOURCE: Cancer Res. (1992), 52(22), 6413-17
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Genetically engineered single-chain Fvs (sFv) are defined as recombinant proteins composed of a variable light chain amino acid sequence of an Ig tethered to a variable heavy chain sequence by a designed peptide. Previous studies using iodine-labeled sFv, derived from the anticarcinoma monoclonal antibody CC49, showed that the 125I-sFv could efficiently target antigen-pos. tumors in a human tumor xenograft model while demonstrating rapid plasma clearance and

minimal uptake in normal organs. One of the issues raised in the anal. of the iodinated sFv metabolic studies was whether similar metabolic patterns would be obsd. if the sFv were labeled with a radiometal. In the studies reported here, 125I-CC49 sFv and 177Lu-CC49 sFv were coinjected in mice bearing antigen-pos. human carcinoma xenografts. Both sFv forms showed similar tumor targeting and plasma clearance pharmacokinetics. The 177Lu-sFv, however, showed a greater uptake in liver and spleen and a much higher uptake in kidney. These studies thus demonstrate that despite their small size (Mr 27,000), the metal-**chelated** sFv shows a metabolic pattern very different than that of the iodinated sFv, which is most likely due to retention of the metal by organs metabolizing the sFv.

L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1983:610522 CAPLUS
DOCUMENT NUMBER: 99:210522
TITLE: Intracellular injections of EGTA block induction of hippocampal long-term potentiation
AUTHOR(S): Lynch, Gary; Larson, John; Kelso, Stephen; Barrionuevo, German; **Schottler, Frank**
CORPORATE SOURCE: Cent. Neurobiol. Learn. Mem., Univ. California, Irvine, CA, 92717, USA
SOURCE: Nature (London) (1983), 305(5936), 719-21
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intracellular injection of the Ca2+ **chelator** EGTA blocked the development of long-term potentiation in slices of rat hippocampus; however, there were no detectable effects on the resting membrane potential, membrane impedance, or the excitatory postsynaptic potential amplitude before high-frequency stimulation. Possibly, EGTA, by buffering intracellular Ca2+, prevents the activation of the enzyme machinery controlling postsynaptic receptors and thereby blocks the induction of long-term potentiation.

L5 ANSWER 5 OF 7 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1973:466454 CAPLUS
DOCUMENT NUMBER: 79:66454
TITLE: Silicon complexes. VII. **Chelate** complexes of silicon with keto enolates and similar ligands
AUTHOR(S): **Schott, G.**; Golz, Karin
CORPORATE SOURCE: Sekt. Chem., Univ. Rostock, Rostock, E. Ger.
SOURCE: Z. Anorg. Allg. Chem. (1973), 399(1), 7-24
CODEN: ZAACAB
DOCUMENT TYPE: Journal
LANGUAGE: German
AB RSiCl3 (R = Me, CH2:CH, ClCH2, Ph) reacted HL (HL = acetylacetone, benzoylacetone, dibenzoylmethane, and benzoylacetanilide) to give [RSiL2]+Cl-, which were easily converted into [RSiL2]+X- (X = HCl2-, FeCl4-, SnCl5-). The latter fact and ir and uv data indicated the ionic character of the complexes with penta-coordinated Si. [SiL3]+Cl-[HL1 = 2-hydroxyacetophenone, 1-nitroso-2-naphthol, 2-nitroso-1-naphthol, and Bz(Ph)NOH], [SiL13]+HCl2-, SiL12Cl2, and ClCH2SiL12X1 (X1 = Cl- HCl2-) were obtained from SiCl4 or ClCH2SiCl3 and HL1.

L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1971:476909 CAPLUS
DOCUMENT NUMBER: 75:76909

TITLE: Silicon complexes. V. **Chelate** complexes of monoorganotrihalosilanes with .beta.-diketones
AUTHOR(S): **Schott, G.**; Golz, Karin
CORPORATE SOURCE: Sekt. Chem., Univ. Rostock, Rostock, Ger.
SOURCE: Z. Anorg. Allg. Chem. (1971), 383(3), 314-20
CODEN: ZAACAB
DOCUMENT TYPE: Journal
LANGUAGE: German
AB MeSiFCl2 and RSiCl3 (R = Me, ClCH2, Ph) reacted with HL (HL = acetylacetone, benzoylacetone, dibenzoylmethane) to give [RSiL2]+ which were isolated as the chloride, HCl2-, FeCl4-, SnCl5-, and picrate. The complexes were characterized by ir and uv spectra.

L5 ANSWER 7 OF 7 CAPLUS COPYRIGHT 1996 ACS
ACCESSION NUMBER: 1970:21741 CAPLUS
DOCUMENT NUMBER: 72:21741
TITLE: Silicon complexes. IV. Formation of **chelate** complexes of silicon with ethyl benzoylacetate
AUTHOR(S): **Schott, Guenther**; Kibbel, H. U.; Hildebrandt, W.
CORPORATE SOURCE: Univ. Rostock, Rostock, Ger.
SOURCE: Z. Anorg. Allg. Chem. (1969), 371(1-2), 81-7
CODEN: ZAACAB
DOCUMENT TYPE: Journal
LANGUAGE: German
AB SiCl4, RSiCl3, RSiCl2(OAc), R2SiCl2, or R3SiCl (R = Me, Et) react with BzCH2CO2Et (HL) to give (SiL3)HCl2, RSiL2Cl, RSiL2(OAc), R2SiL2, and R3SiL, resp., which were characterized by uv and ir spectroscopy.

```
=> s l5 and dota
          195 DOTA
L7          0 L5 AND DOTA

=> s l5 and dota?
          309 DOTA?
L8          0 L5 AND DOTA?

=> s l5 and dtpa?
         5142 DTPA?
L9          0 L5 AND DTPA?

=> d his

     (FILE 'HOME' ENTERED AT 12:24:09 ON 17 SEP 96)

     FILE 'CAPLUS' ENTERED AT 12:24:16 ON 17 SEP 96
L1          0 S SCHOTT/AU
L2       1532 S SCHOTT?/AU
L3       5135 S L2 AND DOTA OR DTPA
L4          0 S L2 AND (DOTA OR DTPA)
L5          7 S L2 AND CHELAT?
L6          0 S L5 AND RADIO ISOTOP?
L7          0 S L5 AND DOTA
L8          0 S L5 AND DOTA?
L9          0 S L5 AND DTPA?

=> s l5 and diamine?
        30988 DIAMINE?
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